RESEARCH

Equipoise in Management of Patients With Acute Symptomatic Carotid Stenosis (Hot Carotid)

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Abstract

Objective

To explore differences in antithrombotic management of patients with acutely symptomatic carotid stenosis ("hot carotid") awaiting revascularization with endarterectomy or stenting (CEA/CAS).

Methods

We used a worldwide electronic survey with practice-related questions and clinical questions about 3 representative scenarios. Respondents chose their preferred antithrombotic regimen (1) in general, (2) if the patient was already on aspirin, or (3) had associated intraluminal thrombus (ILT) and identified clinical/imaging factors that increased or decreased their enthusiasm for additional antithrombotic agents. Responses among different groups were compared using multivariable logistic regression.

Results

We received 668 responses from 71 countries. The majority favored CT angiography (70.2%) to evaluate carotid stenosis, CEA (69.1%) over CAS, an aspirin-containing regimen (88.5%), and a clopidogrel-containing regimen (64.4%) if already on aspirin. Whereas diverse antithrombotic regimens were chosen, monotherapy was favored by 54.4%–70.6% of respondents across 3 scenarios. The preferred dual therapy was low-dose aspirin (75–100 mg) plus clopidogrel (22.2%) or high-dose aspirin (160–325 mg) plus clopidogrel if already on aspirin (12.2%). Respondents favoring CAS more often chose ≥2 agents (adjusted odds ratio [aOR] vs CEA: 2.00, 95% confidence interval 1.36–2.95, $p = 0.001$) or clopidogrel-containing regimens (aOR: 1.77, 1.16–2.70, $p = 0.008$). Regional differences included respondents from Europe less commonly choosing multiple agents if already on aspirin (aOR vs United States/Canada: 0.57, 0.35–0.93, $p = 0.023$), those from Asia more often favoring multiple agents (aOR: 1.95, 1.11–3.43, $p = 0.020$), vs those from the United States/Canada preferentially choosing heparin-containing regimens with ILT (aOR vs rest: 3.35, 2.23–5.03, $p < 0.001$). Factors increasing enthusiasm for ≥2 antithrombotics included multiple TIAs (57.2%), ILT (58.5%), and ulcerated plaque (57.4%); 56.3% identified MRI microbleeds as decreasing enthusiasm.

Conclusions

Our results highlight the heterogeneous management and community equipoise surrounding optimal antithrombotic regimens for hot carotids.

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Carotid atherosclerosis accounts for 15%–20% of ischemic strokes and TIA.[1–3] In a pooled analysis of 3 prospective studies (2 registries and 1 population based), about 24% of patients with symptomatic 50%–99% carotid stenosis had ipsilateral recurrent ischemic events in the first 14 days pre-revascularization.[4] Such patients accounted for 37% of recurrent strokes within 7 days of the initial event in a meta-analysis of population-based studies.[5] Revascularization of symptomatic carotid stenosis via endarterectomy (CEA) is therefore time sensitive—most beneficial within 2 weeks of the last event—with stenting (CAS) being an alternative strategy.[6,7] This urgency confronts the neurologist treating patients with a "hot carotid," defined pragmatically as a recent stroke/TIA (within hours-days of symptom onset) thought to be etiologically related to carotid stenosis.[8]

The optimal antithrombotic regimen for patients with a hot carotid is unknown, particularly as they await CEA/CAS, the key trade-off being between optimizing recurrent ischemic stroke prevention vs minimizing hemorrhagic risk. The Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) and Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) trials have shown a lower risk of major ischemic events with dual antiplatelet therapy (DAPT) using clopidogrel plus aspirin vs aspirin alone for 21 and 90 days, respectively, in a broad population with minor stroke/TIA, with most recurrent events occurring within 1 week.[9,10] However, there was a greater risk of major hemorrhage with 90 days of DAPT in the POINT trial; a meta-analysis of CHANCE and POINT concluded that the benefit of DAPT appeared confined to the first 21 days.[11] Patients with hot carotids were, however, excluded from these trials by design. Trials of intracranial atherosclerosis (ICAS) have shown that warfarin carries greater harm and no benefit over aspirin[12] and that aggressive medical management with DAPT, statin, and blood pressure control confers a low risk of recurrent events.[12,13] A subgroup analysis of CHANCE found that the effects of DAPT vs aspirin alone in reducing stroke recurrence risk or leading to hemorrhage were not significantly different between patients with TIA/stroke with/without ICAS.[14] The generalizability of these findings to patients with cervical carotid atherosclerosis is uncertain. A recent meta-analysis[15] of 7 observational studies and 3 randomized-controlled trials (RCTs)[16–18] comparing outcomes of single vs DAPT in CEA/CAS found that DAPT reduced the risk of TIA (not stroke) in patients undergoing CAS, but was associated with increased bleeding in those undergoing CEA. However, the overall quality of evidence was low to moderate. Uncertainty is heightened when one considers using alternative antiplatelet agents such as ticlopidine[17] or ticagrelor,[19] or combining or substituting with pre-/perioperative anticoagulation (heparin, warfarin, or direct oral anticoagulants),[20] all carrying their own balance of risks vs benefits and often not specifically studied in the hot carotid setting. Decision making is further complicated when intraluminal thrombi (ILT) are seen on vessel imaging.[21,22]

Given these uncertainties, we recently interviewed experts from 3 continents regarding how to manage patients with a hot carotid awaiting CEA/CAS.[23] The experts preferred CT angiography (CTA) for carotid imaging and CEA for revascularization. While noting the potential benefit of DAPT in preventing recurrent events, they recognized varying preferences of surgeons in this regard, with patients sometimes reverting to aspirin perioperatively. They generally favored anticoagulation plus aspirin in patients with ILT but differed on the type and duration of anticoagulation. A more quantitative understanding of how clinicians differ in their approach to hot carotids can help inform the design of future RCTs by highlighting enduring areas of uncertainty. Therefore, we explored practice differences in hot carotid management using a worldwide electronic survey.

Methods

Survey

The survey was launched by the Practice Current section of *Neurology® Clinical Practice* (neurology.org/collection/practice_current). We used an electronic survey with 10 clinical and 7 demographic questions (appendix e-1, links.lww.com/CPJ/A166). The clinical questions pertained to a representative case of a 65-year-old patient presenting with acute-onset right-sided weakness lasting several hours, found to have 80% left-sided extracranial internal carotid artery stenosis. After appropriate hyperacute management, a plan is made for revascularization (CEA/CAS) within the next week, and a statin is started. Respondents were asked about (1) the preferred imaging modality for evaluating the presence and extent of carotid stenosis, (2) preferred revascularization procedure, (3) typical wait time for revascularization, (4) typically favored antithrombotic agent(s), (5) favored agent(s) if the patient was already on low-dose aspirin, (6) favored agent(s) in the presence of ILT, (7) clinical and (8) imaging features that would increase their enthusiasm for additional antithrombotic agents beyond single antiplatelet, and (9) clinical and (10) imaging features that would decrease their enthusiasm for additional agents.

Demographic questions included population treated (adults/children/both), years in practice, work setting, training level, and practice location. The survey was available online and was anonymous. Participation did not require membership in the American Academy of Neurology (AAN) or subscription to AAN journals. No compensation was offered. A link to the questionnaire was available in the *Neurology®* journal web pages, in online ads and the print version of the journals, and in the Practice Current dedicated web page. The survey was also advertised by the AAN and *Neurology®* journals via social media. Individual Internet protocol address was collected to ensure response authenticity. We opened the survey from September 6, 2018, to November 10, 2019, and all responses collected were included in the analysis.

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Statistical analysis

Besides summary statistics, the frequency of responses for each question/scenario was compared for different groups, focusing on (1) preferred revascularization strategy (CEA vs CAS) (2) typical CEA/CAS wait time (2–3 days, 3–7 days, and >7 days), (3) years in practice (trainee, <10-year experience, and >10-year experience), and (4) practice location (United States/Canada, Latin America, Europe, Asia, Africa, and Australia/Oceania). Specifically, we examined the proportion of respondents by years in practice and location who preferred (1) CTA over other imaging modalities and (2) CEA over CAS. We then examined the proportion of respondents by preferred revascularization strategy, years in practice, and location who reported wait times >7 days. We then examined the proportion of respondents in all 4 groupings of interest who (1) chose ≥2 antithrombotic agents in each of the 3 hot carotid scenarios (general presentation, if the patient was already on single antiplatelet therapy, or if there was ILT), (2) chose a regimen containing the most popular agent in each of the scenarios, and (3) identified each clinical/imaging factor as increasing/decreasing their enthusiasm for using additional agents beyond single antiplatelet and statin therapy.

Whereas low-dose aspirin was specified in our survey as 75–81 mg and high-dose aspirin as 160–325 mg, several respondents specified 100 mg of aspirin as their preferred antithrombotic (on selecting the "Other" option); therefore, we expanded our definition of low-dose aspirin to include 75–100 mg for our analyses.

For univariable analysis, we used the Fisher exact test. After identifying differences between the groups with $p < 0.05$ on univariable analysis, multivariable logistic regression was performed to adjust for all confounding variables. Statistical significance was set at 2-sided $p < 0.050$. Analyses were performed using STATA 13.1.

Standard Protocol Approvals, Registrations, and Patient Consents

The study was certified as exempt from review by the Children's National Medical Center Institutional Review Board.

Data Availability

Requests for access to the data used in this article will be considered by the corresponding author.

Results

We received 668 responses from 71 countries, of which 561 (84.0%) were complete (respondent characteristics in table 1). Most respondents preferred CTA to determine significant carotid atherosclerosis (table 2). Of note, 46.9% preferred to use more than 1 imaging modality, the most popular combination being ultrasound and CTA (32.8%). Respondents outside the United States/Canada were less likely to favor CTA, although it remained the most popular option overall in each region (e.g., Latin America, adjusted odds ratio [aOR] [adjusted for years in practice and region]: 0.35, 95% confidence interval 0.19–0.64, $p = 0.001$, table e-1, links.lww.com/CPJ/A165). CEA was favored over CAS by 69.1% of respondents (table 3). Respondents outside the United States/Canada were less likely to favor CEA—although it remained the more popular choice in all regions—with the discrepancy being greatest among respondents from Asia (53.7% preferring CEA vs 83.7% in the United States/Canada, $p = 0.001$, table e-2, links.lww.com/CPJ/A165). Respondents reported longer wait times for CAS (e.g., >7 days: 45.7% for CAS vs 31.8% for CEA, $p < 0.001$) with respondents outside the United States/Canada more likely to report wait times >7 days in multivariable analyses (e.g., Asia aOR [adjusted for preferred revascularization, years in practice, region]: 5.35, 2.99–9.59, $p < 0.001$, table e-3, links.lww.com/CPJ/A165).

When asked about preferred antithrombotic agent(s) for a patient with a hot carotid awaiting revascularization, 561 (88.5%) proposed a regimen containing aspirin (low dose/75–100 mg or high dose/160–325 mg). Most respondents preferred using a single agent (54.4%, table 4), the most common choice being high-dose aspirin (25.6%). Of note, 41.3% preferred dual therapy, and 3.6% preferred triple therapy; the most common combination was low-dose aspirin with clopidogrel (22.2%), although a wide variety of regimens were chosen (table e-4, links.lww.com/CPJ/A165). Those preferring CAS more often chose ≥2 antithrombotic agents (55.6% vs 40.6%, $p = 0.001$; aOR [adjusted for preferred revascularization, wait time, years in practice, region]: 2.00, 1.36–2.95, $p = 0.001$, table e-5, links.lww.com/CPJ/A165). Respondents from Australia less often chose a regimen with high-dose aspirin than those from the United States/Canada (7.1% vs 41.4%, aOR: 0.12, 0.01–0.92, $p = 0.042$, table e-6, links.lww.com/CPJ/A165).

When asked what they would use if the patient was already on low-dose aspirin before their event, 407 (64.4%) respondents selected a regimen containing clopidogrel. 70.6% still chose a single antithrombotic agent, the top choices being clopidogrel (38.4%) and high-dose aspirin (14.4%). 26.0% chose dual therapy, most commonly high-dose aspirin and clopidogrel (12.2%, table 4), and 2.4% chose triple therapy. On multivariable analyses, respondents in Europe less often chose ≥2 antithrombotic agents vs those in the United States/Canada (aOR: 0.57, 0.35–0.93, $p = 0.023$, table e-7, links.lww.com/CPJ/A165). Respondents preferring CAS (aOR: 1.77, 1.16–2.70, $p = 0.008$) and reporting longer wait times (aOR for wait > 3 days vs 2–3 days: 1.60, 1.06–2.40, $p = 0.024$) were more likely to choose a clopidogrel-containing regimen (table e-8, links.lww.com/CPJ/A165).

When asked what they would use if there was an ILT associated with the hot carotid, the most popular regimen was one containing heparin (35.4%). Most respondents still chose 1 antithrombotic agent (67.0%), with heparin monotherapy favored by 27.2%. Of note, 26.0% chose dual therapy, most commonly low-dose ASA and clopidogrel (10.4%, table e-4, links.lww.com/CPJ/A165), and 4.1% chose triple therapy. On multivariable analyses, respondents in Asia were more likely to

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Table 1 Characteristics of the Survey Respondents

Characteristic	N (%)
Patient population treated	Available for 570/668 (85.3)
Adults (18 y and older)	518 (90.1)
Children (0–18 y)	3 (0.5)
Both adults and children	49 (8.6)
Years in practice	Available for 570/668 (85.3)
Less than 10 y	256 (44.9)
10 or more years	181 (31.8)
In training	133 (23.3)
Primary work setting	Available for 567/668 (84.9)
Hospital based	466 (82.2)
Outpatient based	101 (17.8)
Region (based on the country of practice or IP address location if practice not reported)	Available for 668/688 (100)
United States/Canada	183 (27.4)
Europe	213 (31.9)
Australia	15 (2.3)
Latin America	111 (16.6)
Asia	130 (19.5)
Africa	16 (2.4)
Country of practice (top 10)	Available for 561/668 (84.0)
United States	142 (24.3)
Spain	42 (7.5)
Brazil	40 (7.1)
India	40 (7.1)
Germany	26 (4.6)
Chile	17 (3.0)
Australia	16 (2.9)
Romania	15 (2.7)
Canada	13 (2.3)
United Kingdom	11 (2.0)

Abbreviation: IP = internet protocol.

Table 2 Preferred Imaging Modalities (644 Respondents)

	N (%)
Imaging modality	
CTA	452 (70.2)
Ultrasound	345 (53.6)
MRA	106 (16.5)
DSA	73 (11.3)
Using >1 modality	302 (46.9)
Ultrasound and CTA	211 (32.8)
Ultrasound and MRA	59 (9.2)
CTA and MRA	42 (6.5)
Ultrasound and DSA	25 (3.9)
CTA and DSA	22 (3.4)
MRA and DSA	6 (0.9)

Abbreviations: CTA = CT angiography; DSA = digital subtraction angiography; MRA = MR angiography.

choose ≥2 antithrombotic agents than those in the United States/Canada (40.0% vs 26.6%, aOR: 1.95, 1.11–3.43, p = 0.020, table e-9, links.lww.com/CPJ/A165). Respondents practicing outside the United States/Canada were less likely to choose a heparin-containing regimen (table e-10, links.lww.com/CPJ/A165).

When asked what clinical and imaging factors would increase their enthusiasm to use additional antithrombotic agents beyond single angle-platelet therapy, the most favored clinical factors were the patient having multiple TIAs in that carotid territory, already being on an antithrombotic agent, and awaiting CAS rather vs CEA (table 5). The most popular imaging factors were ILT, ulcerated plaque, and microembolic signals on transcranial Doppler (TCD). On multivariable analysis, respondents who preferred CAS more often identified the decision to pursue CAS (vs CEA), echolucent plaque, and atherosclerotic disease in other arteries as increasing their enthusiasm for additional agents (table e-11, links.lww.com/CPJ/A165). Respondents reporting revascularization wait times >7 days more often identified being on an antithrombotic premorbidly as increasing their enthusiasm for additional agents, but less often identified stenting as a relevant factor. Respondents reporting more years of independent practice more often identified multiple TIAs in the same territory, microembolic signals on TCD, echolucent plaque, ILT, and tandem intracranial disease as relevant factors.

When asked what clinical and imaging factors would decrease their enthusiasm for additional antithrombotic agents beyond single angle-platelet therapy, the most favored clinical factors were receiving IV alteplase (although we specified this was >24 hours prior), awaiting CEA and not CAS, and CEA/CAS anticipated to occur within 2 days (table 6). The most favored imaging factors were microbleeds on MRI (56.3%), lesser degree of stenosis (33.9%), and larger vs smaller infarct on imaging (33.7%). On multivariable analysis, respondents preferring CAS were more likely to identify female sex and decision to pursue CEA (vs CAS) as decreasing their enthusiasm for additional agents (table e-12, links.lww.com/CPJ/A165). Respondents reporting more years of independent practice more often identified female sex, isolated ocular

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The choice of the revascularization procedure appears to influence antithrombotic therapy because respondents favoring CAS more often chose multiple antithrombotic agents.

symptoms, smooth stenosis, and larger infarct as decreasing their enthusiasm for additional agents.

Results of Testing for Internal Consistency

On testing for internal consistency in responses, 73.7% of respondents who preferred CAS, and identified CAS (vs CEA) as increasing their enthusiasm for using more than just single antiplatelet and statin therapy, also chose ≥2 antithrombotic agents in ≥1 scenario. Of note, 69.7% of respondents who reported wait times of 2–3 days and identified wait times of 2 days as decreasing their enthusiasm for additional agents chose only 1 agent on all scenarios, as did 53.5% of respondents who preferred CEA and identified the decision to pursue CEA as lowering their enthusiasm for additional agents.

However, only 35.3% of respondents who identified already being on an antithrombotic agent as increasing their enthusiasm for aggressive antithrombotic therapy, and 34.0% of respondents who identified ILT as doing the same, actually chose ≥2 agents for the scenarios with the patient on aspirin premorbidly and with associated ILT, respectively.

Discussion

Practice patterns can become established in medicine even with inadequate evidence. Identifying areas of agreement and disagreement may help clinicians critically examine and refine their own practice patterns, in addition to informing further studies in this area. In this large Practice Current worldwide survey of neurologists, we identified considerable heterogeneity in the medical management of hot carotids. Our results have implications for the design of future RCTs.

First, our findings that CTA (potentially combined with ultrasound) is the preferred method of evaluating carotid stenosis and that CEA is the preferred revascularization strategy for the vast majority of respondents offer a common ground for building further strategies for hot carotid management. In such an environment, a study of periprocedural antithrombotic management that requires MRI-based evaluation or only examines patients awaiting CAS may struggle to gain traction. CTA would suffice to identify ulcerated plaque—identified by the majority of respondents as increasing their enthusiasm for more aggressive antithrombotic therapy—which could be incorporated into studies of risk-stratified therapy. However, CT would not detect microbleeds, identified by the majority of respondents as decreasing their enthusiasm for additional antithrombotic agents, although only 16.5% reported using MRI.

Second, the choice of the revascularization procedure appears to influence antithrombotic therapy because respondents favoring CAS more often chose multiple antithrombotic agents. Respondents reported longer wait times for CAS vs CEA, which may have encouraged more aggressive antithrombotic therapy, but wait times had an inconsistent association with antithrombotic choices in our study. The preferred antithrombotic therapy may be driven more by what is perceived as appropriate preparation for the procedure than by what is considered best medical management for stroke prevention. The observed difference may also relate to greater perceived harm of more aggressive antithrombotic regimens with CEA,[24,25] greater perceived thromboembolic risk with CAS,[7] or challenges with accommodating surgeon preferences in CEA. The rationale driving these clinical decisions merits further investigation, perhaps by in-depth qualitative interviews.

Third, our results demonstrate that despite the high upfront risk of recurrent events and the rise of short-term DAPT for secondary prevention, monotherapy is still preferred by most

Table 3 Preferred Revascularization Strategy and Typical Wait Times for Revascularization for Patients With Acutely Symptomatic Carotid Stenosis, as Reported by Surveyed Clinicians

Preferred revascularization procedure	N (%)	Wait time, <3 d	Wait time, 3–7 d	Wait time, >7 d	*p* Value (Fisher exact)
Total respondents	641	169 (26.4)	243 (38.0)	228 (35.6)	0.001 (across all modalities)
Carotid endarterectomy	443 (69.1)	133 (30.0)	169 (38.2)	141 (31.8)	<0.001 (endarterectomy vs stenting)
Carotid stenting	185 (28.9)	31 (16.9)	69 (37.5)	84 (45.7)	
Did not commit or cited unknown factors (e.g., surgeon preference and anatomy)	13 (2.0)	5 (38.5)	5 (38.5)	3 (23.1)	

All percentages in the first column add to 100%, whereas the remaining percentages in each row add to 100%.

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Our results highlight key regional variations in hot carotid management, which merit being addressed within the design of multicenter RCTs and/or quality improvement initiatives.

clinicians managing a hot carotid, even in the setting of premorbid antiplatelet therapy or ILT. This was despite ILT being identified by the majority of respondents as a factor encouraging them to use more than just single antiplatelet therapy. The most favored monotherapy was aspirin, the benefit of which is well established for secondary prevention,[26] but respondents were split between using low dose (75–100 mg) or high dose (160–325 mg) formulations. This variable dosing has implications for the relative safety and efficacy of aspirin in patients with different body sizes and is itself an avenue for further study.[27] When dual therapy was chosen, the most favored combination was low-dose aspirin plus clopidogrel (DAPT), with high-dose aspirin favored if the patient was already on aspirin premorbidly. This implies that future RCTs comparing antithrombotic strategies in patients with hot carotids will likely need to include high-dose aspirin or DAPT as a comparator arm to receive buy-in from physician stakeholders.

Fourth, our results highlight key regional variations in hot carotid management, which merit being addressed within the design of multicenter RCTs and/or quality improvement initiatives. Such differences included a greater preference for CAS among respondents from Asia (although CEA was still favored by a majority) and longer wait times for revascularization reported by those outside the United States/Canada. Given the urgency of carotid revascularization with symptomatic stenosis, improving wait times should be an important worldwide priority.[28–30] Key regional differences in antithrombotic regimens included respondents from Europe less commonly choosing multiple agents if already on aspirin, those from Asia more often favoring multiple agents, vs those from the United States/Canada preferentially choosing heparin-containing regimens in the setting of ILT. Accommodating and/or accounting for these preferences can help RCTs optimize enrollment or anticipate differential enrollment rates in different regions, depending on the regimens permitted.

Although our analysis has several strengths, including a large worldwide sample, representation of various practice settings and levels of experience, and inclusion of some checks of internal consistency of the responses, there are important shortcomings. First, we could not represent the full spectrum of hot carotid presentations and treatment conundrums needed for more granular analyses of physician decision making. However, we decided to use 3 brief scenarios to maximize survey completion and included additional questions regarding clinical/imaging factors that would influence the respondents' choices to further understand their rationale. Even so, we could not determine the influence that factors such as the patient's ethnicity, comorbidities, neurologic findings, functional status, acute stroke treatments received, the method of determination of the degree of carotid stenosis, or genetic polymorphisms (such as in CYP2C19) may have on respondents' antithrombotic choices. For instance, around 30% of whites and 50%–60% of Asians with stroke/TIA are carriers of the CYP2C19 loss-of-function allele, which may reduce the efficacy of clopidogrel.[31] Second, we cannot be confident whether respondents chose an option because they thought it was the best for the patient or because they felt it would be most

Table 4 Preferred Antithrombotic Agents in Patients With Acutely Symptomatic Carotid Stenosis While Awaiting Revascularization

	Preferred antithrombotic agent(s) in general (N = 634)	If patient is already on low-dose ASA (N = 632)	If intraluminal thrombus is present (N = 628)
Regimen contained:			
Low-dose ASA (75 to 100 mg)	279 (44.0)	126 (19.9)	116 (18.5)
High-dose ASA (160 to 325 mg)	**288 (45.4)**	174 (27.5)	119 (19.0)
Clopidogrel	280 (44.2)	**407 (64.4)**	163 (26.0)
LMWH	35 (5.5)	39 (6.2)	148 (23.6)
Heparin	29 (4.6)	34 (5.4)	**222 (35.4)**
DOAC	11 (1.7)	16 (2.5)	50 (8.0)
Ticagrelor	10 (1.6)	12 (1.9)	8 (1.3)
Cilostazol	8 (1.3)	11 (1.7)	8 (1.3)
Argatroban	1 (0.2)	1 (0.2)	1 (0.2)
No. of antithrombotics (total)			
1	**345 (54.4)**	**446 (70.6)**	**421 (67.0)**
2	262 (41.3)	164 (26.0)	163 (26.0)
3	23 (3.6)	15 (2.4)	26 (4.1)
4	0	0	2 (0.3)
None	4 (0.6)	7 (1.1)	8 (1.3)

Abbreviations: ASA = acetylsalicylic acid (aspirin); DOAC = direct-acting oral anticoagulant; LMWH = low-molecular-weight heparin.
Bold values represent the most preferred anti-thrombotic agent and the most common number of anti-thrombotics selected by respondents in each scenario (column).

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Table 5 Factors Reported by Respondents as Increasing Their Enthusiasm for Using Additional Agents Beyond a Single Antiplatelet and Statin Therapy

	N (%)
Clinical factors	621 responses
Younger age (less than 55 y)	109 (17.6)
Male sex	59 (9.5)
History of hypertension	86 (13.9)
History of diabetes	130 (20.9)
History of coronary arterial disease	169 (27.2)
Already on an antithrombotic	**276 (44.4)**
Patient had multiple TIAs in this territory	**355 (57.2)**
Patient had a stroke and not a TIA	102 (16.4)
Planned for stenting and not endarterectomy	**209 (33.7)**
None of the above	72 (11.6)
Imaging factors	615 responses
Greater degree of stenosis	177 (28.8)
Microembolic signals on transcranial Doppler	**292 (47.5)**
Echolucent plaque (grayscale median < 15)	133 (21.6)
Intraluminal thrombus	**360 (58.5)**
Ulcerated plaque	**353 (57.4)**
Evidence of atherosclerotic disease in other arteries	99 (16.1)
Tandem intracranial disease	152 (24.7)
None of the above	51 (8.3)

Bold values represent the top 3 favored responses in each group.

Table 6 Factors Reported by Respondents as Decreasing Their Enthusiasm for Using Additional Agents Beyond a Single Sntiplatelet and Statin Therapy

	N (%)
Clinical factors	611 responses
Female sex	45 (7.4)
Patient had a TIA and not a stroke	64 (10.5)
Patient had only ocular symptoms	87 (14.2)
Received IV alteplase (assume more than 24 h prior)	**156 (25.5)**
Received endovascular therapy (assume more than 24 h prior)	89 (14.6)
Endarterectomy/stenting will occur within 2 d	**127 (20.8)**
Planned for endarterectomy and not stenting	**128 (21.0)**
None of the above	**192 (31.4)**
Imaging factors	611 responses
Lesser degree of stenosis	**207 (33.9)**
Smooth stenosis	170 (27.8)
Larger vs smaller infarct on brain imaging	**206 (33.7)**
Lacune-like subcortical stroke	159 (26.0)
Microbleeds on MRI	**344 (56.3)**
None of the above	66 (10.8)

Bold values represent the top 3 favored responses in each group.

feasible within their practice. Third, because we did not contact respondents, we could not verify the veracity of respondents' qualifications (such as being a neurologist) or baseline characteristics. However, by not limiting respondents to our network, we were able to capture a greater diversity of respondents. That being said, parts of the world with fewer respondents are at high risk of not being representative of regional practice, instead reflecting the practice of a select few. Fourth, our exploratory analysis was not adjusted for multiple comparisons, resulting in a risk of type 1 errors. Fifth, we did not include transcarotid artery revascularization in this survey; this approach is gaining acceptance in the vascular surgery community, and it is unknown how its adoption might affect choices of antithrombotic management.[32] We also did not examine the role of best medical management vs revascularization in cases with more intermediate degrees of stenosis or for poor procedural candidates; practice variations in this regard merit exploration in future work. Sixth, given the heterogeneity of the hot carotid patient population—with some patients potentially better suited for CAS vs CEA, some having ILT, etc.—a "one size fits all" approach for antithrombotic therapy may be impractical.

In conclusion, while providing guidance on areas of relative agreement on hot carotid management, the areas of equipoise identified by our study can help inform the design of future RCTs. Such RCTs will need to be guided by an understanding of the practice patterns and attitudes of physician stakeholders, including regional variations, to successfully enroll patients and help resolve practical uncertainties.

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Disclosure

A. Ganesh is a member of the editorial team of *Neurology*; has received speaker honoraria from The Meritas Seminar Series,

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Oxford; has served as a consultant for Adkins Research Group and Genome BC; has received research support from The Rhodes Trust and Wellcome Trust; and holds stock/stock options from SnapDx, TheRounds.ca, and Advanced Health Analytics (AHA Health Ltd). L. Bartolini is a Section Editor for *Neurology: Clinical Practice*. Dr. Bartolini is an employee of the federal government. This manuscript was not a term of his employment, nor did he receive any compensation for the manuscript. R.-J. Singh, A.S. Al-Sultan, D.J.T. Campbell, and J.H. Wong report no disclosures. B.K. Menon is a member of the Editorial Board of *Stroke*, a member of the Program Committee, and lead for the acute nonendovascular section of the International Stroke Conference; has received research support from the Canadian Institute for Health Research and the Heart and Stroke Foundation of Canada; and has a patent pending on systems of triage in acute stroke. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

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Appendix Authors

Name	Location	Contribution
Aravind Ganesh, MD, DPhil	University of Calgary, Canada	Conception and design of the study, analyzed the data, and wrote and revised the manuscript
Luca Bartolini, MD	National Institutes of Health, Bethesda, MD	Conception and design of the study, dissemination of the survey, acquisition of the data, and revision of the manuscript
Ravinder-Jeet Singh, MD	University of Calgary, Canada	Design of the study, analysis, and revision of the manuscript
Abdulaziz S. Al-Sultan, MD, FRCPC	University of Calgary, Canada	Design of the study, analysis, and revision of the manuscript
David J.T. Campbell, MD, PhD, FRCPC	University of Calgary, Canada	Design of the study, analysis, and revision of the manuscript
John H. Wong, MD, MSc, FRCSC	University of Calgary, Canada	Conception and revision of the manuscript
Bijoy K. Menon, MD, MSc, FRCPC	University of Calgary, Canada	Conception, writing, analysis, and revision of the manuscript

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Equipoise in Management of Patients With Acute Symptomatic Carotid Stenosis (Hot Carotid)

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